REMARKS

Claims 20, 21, and 38-56 are pending in this application. Claims 1-19, 22-37, and 57 have been canceled. Claims 20, 21, 38-41, and 56 are withdrawn from consideration, as directed to non-elected inventions, in response to the Restriction Requirement mailed June 16, 2008.

Independent claim 42 has been amended to clarify that individual cells isolated in step (a) each contain at least one transposon insertion site that received a transposon insertion. See, for example, page 49, lines 3-5 and page 58, line 22 of the specification, describing the significance of whether or not genes "receive a transposon insertion" and also describing "at least one transposon insertion in each individual cell." Claim 42 has also been amended to clarify that (i) polynucleotide sequences of these transposon insertion sites are compared in step (c) to the Staphylococcus genomic sequence and (ii) open reading frames in this genomic sequence that are not disrupted by a transposon insertion are used in forming a library of putative essential or important genes in step (d). See, for example, page 10, lines 5-18 describing these steps of comparing sequence information and forming a library.

Claim 43 has been amended to recite the term "genomic sequence," for which antecedent basis is found in amended claim 42.

The claim amendments add no new matter.

Rejections under 35 U.S.C. § 112, ¶ 2

Claims 42-55 have been rejected as indefinite for the reasons given on pages 3 and 4 of the Office Action. As noted above, claim 42 has been amended to clarify that, for individual cells that are isolated, *each* of these individual cells contains at least one transposon insertion site. In addition to the original language in claim 42, reciting "at least one transposon insertion site in each individual cell," this further amendment makes it abundantly clear that the Office

Action's proposed, alternative meaning ("where the individual cells are interpreted to mean a group of cells…[and] the entire group of cells contain at least one transposon insertion site") does not apply.

Likewise, amended claim 42 recites, for added clarification, that a transposon insertion site is a site that *received* a transposon insertion as a result of "mutagenizing a Staphylococcus genome" in step (a). A transposon insertion site is therefore not merely a site "where a transposon is *to be* inserted," according to a different meaning of this term, proposed on page 3 of the Office Action.

Additional amendments to claim 42 obviate the objections to the phrases "said database of transposon insertion sites" and "a database comprising the Staphylococcus genome." As amended, step (c) recites that polynucleotide sequences of transposon insertion sites are compared with the Staphylococcus genomic sequence.

The amendments to claim 42 also address the issue of antecedent basis as noted on page 4 of the Office Action.

Please withdraw the rejections under 35 U.S.C. § 112, ¶2.

Rejection under 35 U.S.C. § 103(a)

The Office Action maintains the rejection of claims 42-55 as obvious under 35 U.S.C. § 103(a) over the combination of Charles *et al.* (WO 01/07651; "Charles") and Haselbeck *et al.* (WO 01/70955; "Haselbeck"). Applicants respectfully traverse.

Claim 42 and its dependent claims 43, 44, and 47-55 are all directed to a method for identifying a library of putative essential or important genes using a High Throughput Transposon Insertion (HTTIM) database. The method comprises (a) mutagenizing a *Staphylococcus* genome with a transposon such that individual cells, each having at least one

transposon insertion site are isolated and (b) collecting and mapping polynucleotide sequences of the transposon insertion sites in each individual cell to form a database of the polynucleotide sequences of transposon insertion sites (HTTIM database). The method further comprises (c) comparing the polynucleotide sequences of transposon insertion sites with the *Staphylococcus* genomic sequence to identify open reading frames (ORFs) that are not disrupted by a transposon insertion and (d) forming a library of putative or important genes from the ORFs that are not disrupted by a transposon.

Claims 45 and 46 depend from claim 42 and further recite that the HTTIM database of polynucleotide sequences, used to identify the library of putative essential or important genes, comprises polynucleotide sequences of at least about 3,000 to about 6,000, or at least about 4,000 to 5,000, transposon insertion sites.

It is black letter law that obviousness requires at least a suggestion of all of the features in a claim. See *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003). The combination of Charles and Haselbeck fails to meet this legal standard, at least because neither reference suggests (i) forming a database of polynucleotide sequences of transposon insertion sites or (ii) comparing these polynucleotide sequences with the Staphylococcus genomic sequence, as claimed.

As the Office Action recognizes, Charles teaches isolating polynucleotide sequences that flank inserted transposons and then hybridizing these sequences with a polynucleotide library from the organism. Charles therefore describes a Transposon Mediated Differential Hybridization (TMDH) method.

> However, the problem with this methodology is that it has a high propensity to lead to false positives, and many essential genes will be missed. Furthermore, the method does not yield any detailed information regarding the loci disrupted by transposons, or whether they were hit more than once.
>
> Specification, page 7, lines 18-21.

In contrast to the claimed invention, the hybridization method described in Charles does not involve obtaining the polynucleotide sequences of transposon insertion sites or using these sequences in a comparison with the organism's genomic sequence.

Haselbeck similarly fails to suggest forming a database of polynucleotide sequences of transposon insertion sites. Haselbeck does not mention transposon insertion at all. In contrast to the disclosures of the cited references, Applicants alone teach the mapping of gene or gene fragment sequences containing transposon insertion sites, and comparing these polynucleotide sequences (numbering, for example, from 3,000 to 8,000) to the bacterial genomic sequence in order to form a library of putative essential or important genes. See, for example, the procedures on page 46, line 20 to page 50, line 2 of the specification. Likewise, the important commercial advantages of the method of the claimed invention over prior art methods such as TMDH are recognized only in Applicants' own specification and nowhere Charles and/or Haselbeck.

Since the combination of Charles and Haselbeck does not suggest the claimed features, *prima facie* obviousness is not established. Please withdraw the rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above amendments remarks, all pending claims of this application are believed to be in condition for allowance. Acknowledgement of the same is respectfully requested. This response is believed to completely address all of the substantive issues raised in the Office Action dated October 28, 2009.

Respectfully submitted,
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